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Clinical Significance of ^{99m}Tc-MIBI Breast Imaging in the Diagnosis of Early Breast Cancer

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OBJECTIVE: To find an effective, sensitive, specific and noninvasive diagnostic method for cancer.

METHODS: 109 masses from 102 patients with breast lesions smaller than 2 cm in diameter were divided into three groups to undergo ^{99m}technetium-methoxyisobutylisonitrile (^{99m}Tc-MIBI) imaging. The results were compared with their pathology. Twenty cases without breast lesions were selected as a control group. Abnormal density of ^{99m}Tc-MIBI in the breast and a threshold level 10% higher than that in the counterpart of the healthy breast was regarded as positive.

RESULTS: Of 32 breast cancers, positive imaging appeared in 25. Negative imaging was found in 31 of 38 benign breast lesions. Of 39 nonpalpable breast lesions, five cases were breast cancers and 34 cases benign. Positive MIBI imaging appeared in all of the breast cancers, while in the benign lesions, four were positive and 30 negative. No positive imaging was found in the control group. The diagnostic accuracy, sensitivity, specificity, positive predictive value and negative predictive value of ^{99m}Tc-MIBI were 88.4%, 89.2%, 88.0%, 75.0% and 95.3%, respectively.

CONCLUSIONS: ^{99m}Tc-MIBI imaging had high sensitivity and accuracy in the diagnosis of breast cancer, as well as in the differentiation between benign and malignant breast lesions. It could provide reliable information in confirming the diagnosis in patients with clinically suspected breast cancer.
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The incidence of breast cancer is increasing in China and it will be the most common malignant tumour in women in the early years of the 21st century.[1] ^{99m}technetium-methoxyisobutylisonitrile (^{99m}Tc-MIBI) breast imaging, an effective, sensitive, specific and noninvasive diagnostic method for breast cancer detection, has been attracting the attention of physicians. From March,1994 to September, 1999, 109 breast masses smaller than 2 cm in diameter (clinically so-called "early breast cancer") in 102 patients in Huashan Hospital were divided into three groups to undergo ^{99m}Tc-MIBI breast imaging and the results were compared with their pathology. Twenty cases without breast lesions were selected as a control group. The results showed that ^{99m}Tc-MIBI breast imaging could provide reliable information for the diagnosis of early breast cancer.

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Materials and Methods

Patient selection and grouping

Breast cancer

32 women with 32 lesions were included in this group. All were married women with an average age of 51.2 years (range, 31 to 81 years). Of 32 lesions, 15 were smaller than 1 cm in diameter and 17 ranged from 1 cm to 2 cm in diameter. Breast cancer was confirmed by histopathology.

Benign lesions

38 lesions in 35 women were included in this group. Among them, 29 were married. The mean age was 40.8 years (range, 15 to 71 years). Sixteen lesions were smaller

than 1 cm in diameter and 22 ranged from 1 cm to 2 cm in diameter. Postoperative pathology showed that 35 were benign breast lesions and three were chronic mastitis or abscesses.

Nonpalpable lesions

35 female patients with 39 lesions were included in this group. 33 patients were married. Their ages ranged from 20 to 46 years, with a mean of 40.1 years. 39 lesions were preoperatively confirmed by ultrasonography. 29 lesions were smaller than 1 cm and 10 were from 1 cm to 2 cm in diameter. 34 benign breast lesions and five breast cancers were confirmed by pathology after surgery.

Controls

20 married women without breast lesions were included in this group. Their mean age was 45.3 years (range, 24 to 72 years).

Instruments and methods

The ELSCINT APEX 409AG SPECT (ELSCINT, Tel Aviv, Israel) device was used to perform ^{99m}Tc-MIBI breast imaging. ^{99m}Tc-MIBI with a marking rate greater than 95% was supplied by Xinke Co., Shanghai, China.

In order to highlight the lesions, the patient was placed in a supine position with both arms held up to keep a wider distance between the breasts and the heart during the examination. The probe faced the breast directly and a pro-oblique or lateral image was taken, if necessary. ^{99m}Tc-MIBI 925WBq was administered intravenously, and early and delayed static images were taken after 5 minutes and 60 minutes, respectively.

Image processing

Static images of the lesions were observed. A region of interest (ROI) was taken in the lesion and in the counterpart of the contralateral breast. The radiological ratio between the tumour and the normal tissue (T/N) was calculated and then compared with that of the contralateral breast. A positive result was considered if the T/N ratio of the lesion was 10% higher than that of contralateral breast; slightly increased ^{99m}Tc-MIBI was considered if the threshold of ^{99m}Tc-MIBI uptake was increased by less than 10% but was higher than that of the contralateral breast—this was also considered positive imaging. Negative imaging was considered when the T/N ratio of the lesion was equal to that of the contralateral breast. In calculations, the highest ratio of T/N was regarded as the diagnostic value whenever early or delayed imaging was taken and regardless of what position the patient took.

RESULTS

The sensitivity, specificity, accuracy, positive and negative predictive value of ^{99m}Tc-MIBI breast imaging was 89.2%, 88.0%, 88.4%, 75.0% and 95.3%, respectively (Table).

In the breast cancer group, positive imaging appeared in 28 cases (including three cases with slightly increased ^{99m}Tc-MIBI breast imaging), and false negative results appeared in four. The diagnostic accuracy was 87.5%.

In the benign group, false positives appeared in seven cases (of them, two had slight increases). The diagnostic accuracy of ^{99m}Tc-MIBI breast imaging in this group was 81.6%. Chronic mastitis was confirmed pathologically in five patients with false positive ^{99m}Tc-MIBI breast imaging.

In the group of nonpalpable breast lesions, breast cancer was confirmed in five out of nine cases with positive ^{99m}Tc-MIBI breast imaging (slightly increased imaging appeared in two). The diagnostic accuracy was 90.0%. Chronic mastitis was confirmed in three patients who were misdiagnosed. In this group, five lesions were nonpalpable but ^{99m}Tc-MIBI breast imaging showed an abnormal accumulation of isotope in the breast. Ultrasound-guided biopsy was performed and the diagnosis of breast cancer was confirmed pathologically.

In the control group, all 20 patients had normal ^{99m}Tc-MIBI breast imaging, although abnormal density of ^{99m}Tc-MIBI in right axillary lymph nodes was found in one patient, in which malignant lymphoma was subsequently confirmed by lymph node biopsy.

Table. Comparison between results of ^{99m}Tc-MIBI breast imaging and pathology

Group	Positive	Negative	Total
Malignant	28	4	32
Benign	7	31	38
Nonpalpable lesion	5	30	39
Control	0	20	20

Discussion

^{99m}Tc-MIBI has an affinity for malignant tumour tissue and, thus, the rate of uptake of ^{99m}Tc-MIBI is higher in breast cancer lesions. When the T/N ratio of ^{99m}Tc-MIBI in the breast was higher than or equal to 10%, this abnormal density could be seen with the naked eye (Figure 1). It was helpful in the clinical diagnosis. After uptake into tissues, ^{99m}Tc-MIBI is rapidly eliminated. High uptake of ^{99m}Tc-MIBI could be seen just 5 minutes after intravenous injection and delayed abnormal accumulation imaging could be observed 1 hour later. Similar results were also reported by Khalkhali et al.[2] The abnormal accumulation disappeared 5 hours later.

Unlike breast cancer, our study showed that early and delayed imaging did not appear in benign breast lesions. The T/N ratio of ^{99m}Tc-MIBI was lower than 10% in patients with benign breast lesions.

The mechanism of ^{99m}Tc-MIBI uptake has not been clearly evaluated. Chiu and colleagues postulated that it might be related to ionic electroaffinity to fat, intracellular mitochondria mass, tumour blood supply and cellular metabolic activity.[3] The blood supply of breast cancer is richer than that of normal breast tissue. The cellular differentiation and metabolism of breast cancer is abnormally active and this may be an important cause of ^{99m}Tc-MIBI uptake in breast cancer.

In our study, false positive imaging was seen in five chronic mastitis patients and two fibroadenoma patients with slightly increased ^{99m}Tc-MIBI. We inferred that false positive imaging might be related to cellular mass and fibrous hyperplasia within these lesions. Waxman et al also reported similar findings.[4] In order to reduce the chance of false positivity in benign lesions, some authors used an accumulating index to differentiate benign lesions from malignant ones.[5]

The causes of false negative results remain undetermined. These might be related to smaller,

Figure 1. ^{99m}Tc-MIBI breast imaging. Abnormal accumulation of ^{99m}Tc-MIBI (round-shaped density) in the lesion of the right breast. Anterior position, taken 5 minutes after intravenous injection of ^{99m}Tc-MIBI.

Figure 2. ^{99m}Tc-MIBI breast imaging. Slight increase of ^{99m}Tc-MIBI in the lesion of the right breast. Anterior position, taken 1 hour after intravenous injection of ^{99m}Tc-MIBI.

deeper lesions in which abnormal accumulation of ^{99m}Tc-MIBI would not be detected by a plain static imaging device.[6] Four false negative ^{99m}Tc-MIBI breast imaging results appeared in lesions smaller than 1 cm in diameter in our study. Smaller volume of tumour cells and /or poor blood supply might also be related to false negativity.[7]

In cases of slightly increased of uptake within the breast (Figure 2), malignant lesions should be seriously considered, and excisional biopsy is recommended.[8] In the present study, two occult lesions with slightly increased of ^{99m}Tc-MIBI uptake were pathologically confirmed to be breast cancer by ultrasound-guided biopsy. Slightly increased ^{99m}Tc-MIBI uptake also appeared in three cancerous lesions. It is worthwhile to excise these lesions in order to rule out malignancy.

In our study, the sensitivity, specificity, positive predictive value and negative predictive value of ^{99m}Tc-MIBI breast imaging was 89.2%, 88.0%, 75.0% and 95.3%, respectively. These data suggest that ^{99m}Tc-MIBI breast imaging would be very helpful in clinical practice for the diagnosis of breast cancer. From the results, we conclude that ^{99m}Tc-MIBI breast imaging is of great significance in the diagnosis of early breast cancer, especially for the differentiation between benign and malignant lesions, as well as for clinically suspicious lesions.

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